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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,652	12/05/2003	Judith Kelleher-Andersson	109015-032	8455

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,652	KELLEHER-ANDERSSON ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed March 10, 2006 presents remarks and arguments to the office action mailed February 08, 2006.

Response to Restriction Requirement

Applicant elects group II with traverse and added claims 19-20. Applicant's election with traverse of Group II in the reply filed on March 10, 2006 is acknowledged. The traversal is on the ground(s) that the newly added claims 19 and 20 are readable upon the elected group. The claims have been added and are hereby examined along with the elected group.

Status of claims

Claims 1-13 and 15-18 are withdrawn.

Claims 19-20 are new.

Claims 14 and 19-20 are pending.

Claim Rejections - 35 USC § 112-Second

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: The claim refers to compound of formula I but fails to show the compound structure or name. Formula 1

is given in the specification but confusingly without any definition of what the R and X moieties are.

II. Claim 14 is also rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What compound of formula I is being referred to?

Claim Rejections - 35 USC § 112-First

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

1) Nature of invention.

2) State of prior art.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

4) Level of predictability in the art.

5) Amount of direction and guidance provided by the inventor.

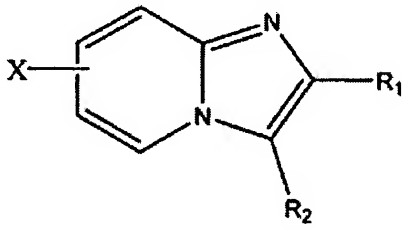
6) Existence of working examples.

7) Breadth of claims.

8) Level of ordinary skill in the art.

See below:

In the instant case, applicants are claiming a method of treating neurodegenerative and neuropsychiatric disorders in a patient administering a fused



imidazole of formula I (claim 14) and as stated in (claim 19) a neurogenic agent sufficient to increase the number of neurons thus implying that a representatives of fuzed imidazole compounds and or representatives of neurogenic compounds are capable of treating all neurodegenerative disorders and/or representatives of neuropsychiatric disorders in a patient.

1) Nature of the invention.

The nature of the invention is methods of treating a patient to alleviate the pathological effects of all neurodegenerative and or neuropsychiatric disorders, comprising administering the instant compound to a patient in need thereof. As stated, however, claims 14 and 19 recite that any or all- neurodegenerative and or neuropsychiatric disorders is intended with any and all imidazole compounds of the above shown structure is capable of treating neurodegenerative disorder and neuropsychiatric disorders.

2) State of the prior art and the predictability or lack thereof in the art.

Applicants' specification (see page 32) indicates large number unknown agents (e.g., protein factors, peptides, nucleic acids, natural compounds, or synthetic compounds) for discovering a candidate drug involves repeating the same test for several screening of a hundreds to several million times. This requires a great deal of reproducibility from the test. In order to obtain the state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibited the desired pharmacological activities (i.e. what compounds can treat which specific disease). The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

Thus, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by compounds of the instant claims, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds due to the unpredictability of the role of the disease.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation as mentioned above. One of ordinary skill in the art would first need to determine the type of

neurodegenerative and or neuropsychiatric disorders to be treated, and then determine which of the thousands of compounds would be suitable for said treatment and/or prevention.

4) Level of predictability in the art.

The art pertaining to the treatment of neurodegenerative and or neuropsychiatric disorders remain highly unpredictable. As disclosed above, treating one disorder does not necessarily result in treating series of related disorders or symptoms even in view of the seemingly high level of skill in the art. Firstly, for a compound or genus to be effective against a disease associated with neurodegenerative and or neuropsychiatric disorders generally is contrary to medical science. neurodegenerative and or neuropsychiatric disorders is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, for example Parkinson's disease, Alzheimer's disease, Multiple sclerosis, Neuropathies, Huntington's disease, Amyotrophic lateral sclerosis (ALS) etc, notwithstanding the types of inhibitors that encompass these Dopamine agonists NDA antagonists New beta interferons Monoclonal antibodies Growth factors Glutamate inhibitors Cell therapy Gene therapy and biochemical pathways that mediate the neurodegenerative and or neuropsychiatric reaction. There is no common mechanism by which, or even most, neurodegenerative and or neuropsychiatric arise, as there is no, and there can be no "one drug" against all neurodegenerative and or neuropsychiatric related diseases generally.

5) Amount of direction and guidance provided by the inventor.

No working example is given on how the drug compound works in a patient. The claim is directed to treating neurodegenerative and or neuropsychiatric disorders in patient. The amount of direction or guidance present is found on pages 38-45 wherein *in vitro* assay was used to identify and evaluate growth of new neurons (nerogenesis). In addition, the gap between *in vitro* activity and *in vivo* utility is large enough to warrant thorough and compelling *in vivo* or clinical data. Notwithstanding this statement, on page 42 of the specification Applicant uses the phrase would be administered thus indicating the uncertainty of the claimed invention.

6) Existence of working examples.

As discussed above no working example is provided. Applicant's limited working example does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention with the numerous variation of the fused imidazole compounds.

7) Breadth of claims.

Claims 14 and 19 are extremely broad due to the vast number of possible diseases encompassed by the instant invention and the vast number of possible variation of the compound.

8) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of any disease. As a result necessitating

one of ordinary skill in the art to perform an exhaustive search to determine which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

Therefore, in view of the Wands factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds encompassed in instant claims, with no assurance of success.

The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms, and treatment (or lack thereof) for neurodegenerative and or neuropsychiatric. It establishes that it is not reasonable to any agent(s) to be able to treat neurodegenerative and or neuropsychiatric generally.

This rejection can be overcome by reciting specific closely related diseases with the specific fused imidazole compound.

II. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The compound structure of formula I (see page 43 of specification) does not specify or give the possible substituents of R or X. Claim14 employing small molecule with the substituents represented by R and X are not described nor exemplified and does not inform the public of the limits of the monopoly asserted.

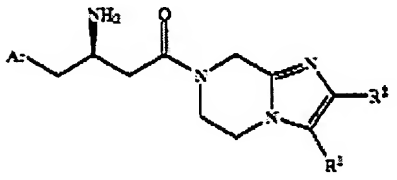
Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14 and 19-20 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Edmondson et al. US 6,699,871 B2.

Edmondson et al. teaches a fused imidazole compound



used in the treatment of neurodegenerative disorders (see col. 9 lines 54+) and psychiatric disorders (see col. 11 lines 10+) as in current claims 14 and 19 in humans (see col. 14 lines 9). It is anticipated that the growth of new neurons will take place.

Claim Rejections - 35 USC § 103

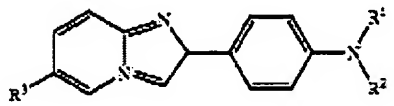
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

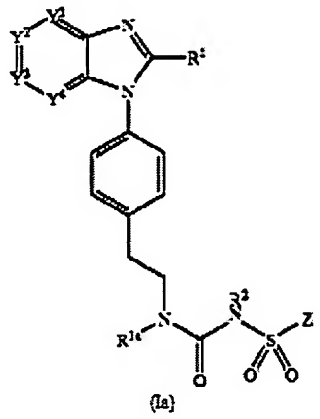
Claims 14, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kung et al., US 2003/0059369 now a patent US 6,96,039 B2 taken with Nakao et al. US 2002/0107273 A1 in view of Edmondson et al. US 6,699,871 B2.

Kung et al. teach the current claim 14 using a compound



an imidazole (see col. 6 lines 45+) to treat inhibition of amyloid deposits that leads to neurodegenerative disorder such as Alzheimers' disease (see col. 1 lines 29+) in a patient (see col. 29 lines 12+) in a human (see col. 29 lines 15+).

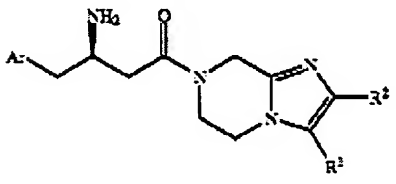
With regards to claim 14, Nakao et al. teach the compound structure of formula



(Ia)

I a fused imidazole (see page 16) a similar structure to the compound NSI 106 as described in the provisional application for the treatment of Alzheimers' disease thus Alzheimer is a neurodegenerative disorder in a mammal. Although the Nakao et al. reference did not per se teach the instant claim 19, in that it did not specifically teach growth of new neurons, however, (see page 48 0584 and 0585) cAMP assay in rat EP4 was done. This type of assay is the response element binding protein, which is known to play an important role in neural survival and plasticity. Increase cell indicates cell proliferation thus neurogenesis.

Edmondson et al. teaches a fused imidazole compound



used in the treatment of neurodegenerative disorders (see col. 9 lines 54+) and psychiatric disorders (see col. 11 lines 10+) as in current claims 14 and 19 in humans (see col. 14 lines 9).

The claims differ from the reference by not reciting growth of new neurons as in the instant claim 19. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use any of the above compounds to treat neurodegenerative disorder and psychiatric disorder because the above references teach that compounds of fused imidazoles are used in the treatment of neurodegenerative disorders and neuropsychiatric disorders as in the claimed invention. If neurodegenerative is defined as relating to the deterioration of nerve tissues, treating Alzheimer will therefore stop the neurodegeneration of the nerve tissues and regenerate new ones absent factual evidence.

One of ordinary skill in the art would have combined the above cited references at the time the claimed invention was made including those of the claims, because an ordinary artisan would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus the same use as the genus as a whole. Since only the genus of the compound was disclosed in the claims it is obvious that a specie falling within the genus would have the same properties.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ardin H. Marschel 5/3/06

SVG
5/8/06

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER